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Differing Oxygen Concentrations and the Effect on Post-Hypoxia Recovery

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14. ABSTRACT

Given the consistent rise in hypoxia-like in-flight emergencies and the negative effects of hypoxia on human performance, it is important to garner a more complete understanding of performance recovery following a hypoxic event. Previous research has reported that use of differing oxygen concentrations following a hypoxic event has resulted in dissimilar recovery profiles. The goals for this study were to examine operator performance on a tracking task and regional oxygen saturation of the frontal lobes of the brain during a hypoxic event and to document differences in performance recovery for two commonly used recovery gas oxygen (O_2) concentrations (100% vs. 21%). Ten subjects completed a tracking task while being exposed to a 25,000-foot equivalent O_2 concentration (~7%) using the reduced oxygen breathing device for 5 minutes. Each exposure was preceded by a 5-minute baseline, with subjects breathing 21% O_2, and was immediately followed by a 5-minute recovery period, during which either 21% or 100% O_2 was administered. Tracking task performance and regional oxygen saturation were surveyed during these periods and for an additional 15 minutes following the exposure and again at 30 minutes and 1, 2, 3, 4, and 24 hours following the exposure to catalogue remaining performance deficits, all while breathing 21% O_2. A repeated measures analysis of variance revealed no significant differences between the speeds at which participants recovered from hypoxic exposure, regardless of which O_2 concentration was used. With regard to tracking task performance, results of this study indicate that participants recover immediately following administration of both the 100% and 21% O_2 recovery gases. Thus, there was no delay in recovery, and the administration of 100% O_2 following the exposure did not lead to increased deficits in performance as previously observed. Regional oxygen saturation values also recovered at similar temporal rates, regardless of recovery gas concentration. However, these values were unsustainable, as they fell below baseline levels during the 30-minute post-exposure examination and remained depressed until the 4-hour post-exposure examination.

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Hypoxia, recovery gas, cognitive performance

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1.0 SUMMARY

Given the consistent rise in hypoxia-like in-flight emergencies and the negative effects of hypoxia on human performance, it is important to garner a more complete understanding of performance recovery following a hypoxic event. Previous research has reported that use of differing oxygen concentrations following a hypoxic event has resulted in dissimilar recovery profiles. The goals for the present study were to examine operator performance on a tracking task and regional oxygen saturation of the frontal lobes of the brain during a hypoxic event and to document differences in performance recovery for two commonly used recovery gas oxygen (O_2) concentrations (100% vs. 21%). Ten subjects completed a tracking task while being exposed to a 25,000-foot equivalent O_2 concentration (~7%) using the reduced oxygen breathing device for 5 minutes. Each exposure was preceded by a 5-minute baseline, with subjects breathing 21% O_2, and was immediately followed by a 5-minute recovery period, during which either 21% or 100% O_2 was administered. Tracking task performance and regional oxygen saturation were surveyed during these periods, as well as for an additional 15 minutes following the exposure and again at 30 minutes, 1 hour, 2 hours, 3 hours, 4 hours, and 24 hours following the exposure to catalogue remaining performance deficits, all while breathing 21% O_2. A repeated measures analysis of variance revealed no significant differences between the speeds at which participants recovered from hypoxic exposure, regardless of which O_2 concentration was used. With regard to tracking task performance, results of this study indicate that participants recover immediately following administration of both the 100% and 21% O_2 recovery gases. Thus, there was no delay in recovery, and the administration of 100% O_2 following the exposure did not lead to increased deficits in performance as previously observed. Regional oxygen saturation values also recovered at similar temporal rates, regardless of recovery gas concentration. However, these values were unsustainable, as they fell below baseline levels during the 30-minute post-exposure examination and remained depressed until the 4-hour post-exposure examination.

2.0 INTRODUCTION

Rapid advances in the fields of aerodynamics, propulsion, and aerospace engineering have allowed aircraft to greatly increase their airspeeds, maneuverability, and operational altitudes. However, these advances in aircraft design have resulted in the imposition of an increasing amount of physiological stress on pilots and aircrew stemming from missions and assignments within these extreme operational environments. Among the leading aeromedical concerns is a lack of consistently supplied and adequately oxygenated breathable air during flight operations, which produces a condition known as “hypoxic hypoxia,” in which perfusion of oxygenated blood in the brain is inhibited [1]. If not corrected in a short amount of time, adverse physiologic changes accompanied by an array of undesirable symptoms can be experienced, including lightheadedness, difficulty concentrating, and diminished perceptual capabilities [2-4], which markedly increase the likelihood of a serious mishap.

Although many of the symptoms of hypoxia are overt and recognizable, the majority of symptoms are insidious and idiosyncratic (e.g., slowed reaction times, impaired task performance) [5-14]. Further, previous research has suggested that perceptual and cognitive abilities may continue in a diminished state for a significant length of time following hypoxic exposure, with intensities associated with the altitude and duration of the exposure [15-17].

In an attempt to understand the effects of hypoxia on reaction time, Phillips and his associates first demonstrated that subjects' performance on a reaction time task failed to return to baseline levels in 10 minutes of post-hypoxic exposure (breathing 21% oxygen [O_2]) [17]. In their initial programmatic investigation regarding this cognitive and perceptual recovery from hypoxic stress, Phillips, Hørning and Funke noted that the aspects of perceptual capability examined, contrast sensitivity and color vision, returned to baseline levels shortly after being presented with sea-level O_2 concentrations (21%). However, neither response time, indexed through both simple and choice reaction time trials, nor regional cerebral oxygen saturation (rSO_2), as measured via near-infrared spectroscopy (NIRS), returned to pre-exposure values until they were assessed 24 hours later, suggesting an impairment of certain physiologic and performance characteristics subsequent to hypoxic exposure [15].

To more closely mimic a valid operational emergency, Phillips and his colleagues followed their earlier investigation with one in which the speed of recovery from hypoxia was tracked for a similar length of time, but 100% O_2 recovery gas was administered in place of the sea-level concentration as used in the abovementioned research. Consistent with expectation, response times were significantly slower during the hypoxic period than those measured during the baseline portion of the task. However, in the time period immediately following hypoxic exposure, during the administration of the 100% O_2 recovery gas, response times were again found to be significantly slower than those recorded during the baseline time period and even the preceding hypoxic time period. During the next examination period, 30 minutes after the initial hypoxic exposure, the recovery gas was replaced with sea-level O_2 and response times returned to baseline levels. Regional O_2 saturation indexed throughout these experimental trials demonstrated a quick return to baseline levels during the 100% O_2 recovery gas administration period. However, this amelioration in rSO_2 values proved to be unsustainable, as the return to baseline levels was immediately followed by a decline to significantly lower O_2 saturation values upon the return to sea-level O_2. In this case, rSO_2 did not fully recover until indexed 24 hours later [16].

At this point, it is clear that current cognitive and physiological evidence is insufficient to completely catalogue the performance decrements and temporal envelope associated with hypoxic exposure and the subsequent recovery therein. Accordingly, the goals for the present study were to assess task performance in concordance with rSO_2 for a longer duration throughout and immediately following a hypoxic event to examine the insult to these functions and the ensuing restoration to pre-exposure levels with differing emergency gas concentrations (21% and 100%). Based on previous studies [15,16], it was anticipated that both cognitive task performance and tissue oxygen saturation would remain depressed for an extended period of time following the hypoxic event. However, it was expected that these metrics would revert to baseline levels significantly more quickly when subjects were administered 100% O_2 when compared to 21% O_2.

3.0 METHODS

3.1 Subjects

Ten active duty military personnel (all male) completed each phase of the experimental protocol. Those with certain pulmonary or vascular medical conditions that could be aggravated by hypoxia exposure, engaging in particular lifestyle choices involving frequent alcohol or

tobacco use, or having resided at an altitude above 5000 feet within the previous 3 months were not considered as potential subjects. Human testing was approved by the Institutional Review Board at the Naval Medical Research Unit – Dayton, and each subject provided written consent to participate prior to study inclusion.

3.2 Equipment

3.2.1 Reduced Oxygen Breathing Device (ROBD-2). The ROBD-2 is a device used to mix breathable gasses, combining bottled air with nitrogen to simulate O_2 values found at altitudes between sea level (21%) and 34,000 feet (4.4%) in a normobaric environment, delivered through a standard aviation flight mask. The ROBD-2 is also capable of providing a supply of 100% O_2, analogous to that used in an emergency situation. For the present study, an altitude of 25,000 feet was selected to test task performance, with an effective fraction of inspired O_2 for that altitude of 7.7%.

3.2.2 Blood Oxygen Saturation. Oxygen saturation at the index finger of the subjects' non-dominant hand was measured with a Datex Ohmeda finger oximeter (GE Healthcare, Chicago, IL) for subject safety. If, at any point during the low-oxygen exposure period, an individual's blood O_2 saturation declined below 55%, the subject would immediately be administered the recovery gas from the condition to which he was assigned.

3.2.3 NIRS. Regional cerebral O_2 saturation was measured from the right hemispheric frontal lobe by an INVOS™ 5100C cerebral oximeter (Medtronic, Minneapolis, MN). The O_2 sensor was placed on the right side of the subject's forehead, superior to the eyebrow. In positioning the sensors, investigators were careful to avoid placement on top of a sinus cavity, which would have resulted in erroneous O_2 values being recorded. To ensure consistency of measurement, the sensor was secured in place with adhesive glue and remained attached to the subject throughout the initial day of testing. Additionally, the distance of the sensors to the midline of the forehead and to the supraorbital foramen was recorded and used to safeguard against misplacement for the ensuing visits.

Regional O_2 saturation values were sampled at a rate of one measurement every 5 seconds and were automatically recorded by the oximeter. As opposed to making use of the absolute saturation levels, variations in rSO_2 were calculated as proportional deviations from each subject's baseline point.

3.2.4 Tracking Task. Of particular relevance to the present study, it has been shown that performance on a complex tracking task is severely impaired during hypoxia, and that error rate increases by up to 200% [18] due to the environmental stress. As such, in the current investigation, participants were asked to perform a tracking task by using a computer joystick to align an independently moving reticle with the center point of a crosshair displayed on the screen. The target appeared in the middle of an otherwise blank field within a computer window, while movement of the controllable reticle was accomplished by assigning a distribution of speeds and directions in which the reticle could travel, appearing to move randomly throughout the task assignment.

Performance was assessed through a calculation of the deviation in location of the moving reticle and the center of the target crosshair 10 times per second during the task. The divergence of the reticle and the target crosshair was expressed in terms of a vector error using the Euclidian distance in pixel units between the location of the reticle and the center point of the target.

3.3 Procedure

Subjects reported to Naval Medical Research Unit – Dayton on four separate occasions: one hypoxic exposure per recovery concentration of O_2 administered (21% and 100%), and then again 24 hours after each exposure for a final performance assessment. Written consent to participate was given by each subject during the initial visit and all study related questions were answered.

During the first visit, the order of recovery gas administration was determined at random, and each subject was given an opportunity to practice the tracking task for 5 minutes prior to the execution of the study protocol. Following this, subjects breathed a sea-level (21%) O_2 concentration for 5 minutes, a 25,000-foot equivalent (7.7%) O_2 concentration for 5 minutes, an emergency gas concentration (either 21% or 100%, depending on order of assignment) for 5 minutes, and finally, an additional 15 minutes of sea-level equivalent O_2, all while continuously performing the tracking task. Performance was then assessed for additional 5-minute periods at intervals of 30 minutes, 1 hour, 2 hours, 3 hours, 4 hours, and 24 hours subsequent to hypoxic exposure. This process was repeated 1 week later, although subjects were administered the alternate concentration of recovery O_2 during this iteration of the study. In sum, during the course of the investigation, each subject performed the tracking task for 60 minutes (30 minutes of continuous performance, followed by six 5-minute assessment periods) for both recovery O_2 concentration profiles, while rSO_2 was regularly sampled every 5 seconds throughout.

4.0 RESULTS

In the ensuing figures, data are presented as the mean ± standard error. Data were analyzed via repeated measures analyses of variance (ANOVAs) with an alpha level set at 0.05. In the event of a significant finding, to account for inflated family-wise error rates, Tukey's honestly significant difference correction was applied to post hoc *t*-tests.

4.1 Tracking Task Performance

Regarding tracking task performance, the geometric mean of the Euclidian distance from the controllable reticle to the center of the target was used to normalize the data, which were positively skewed. The vector errors in both the 21% and 100% recovery gas treatments are plotted as a function of time in Figure 1.

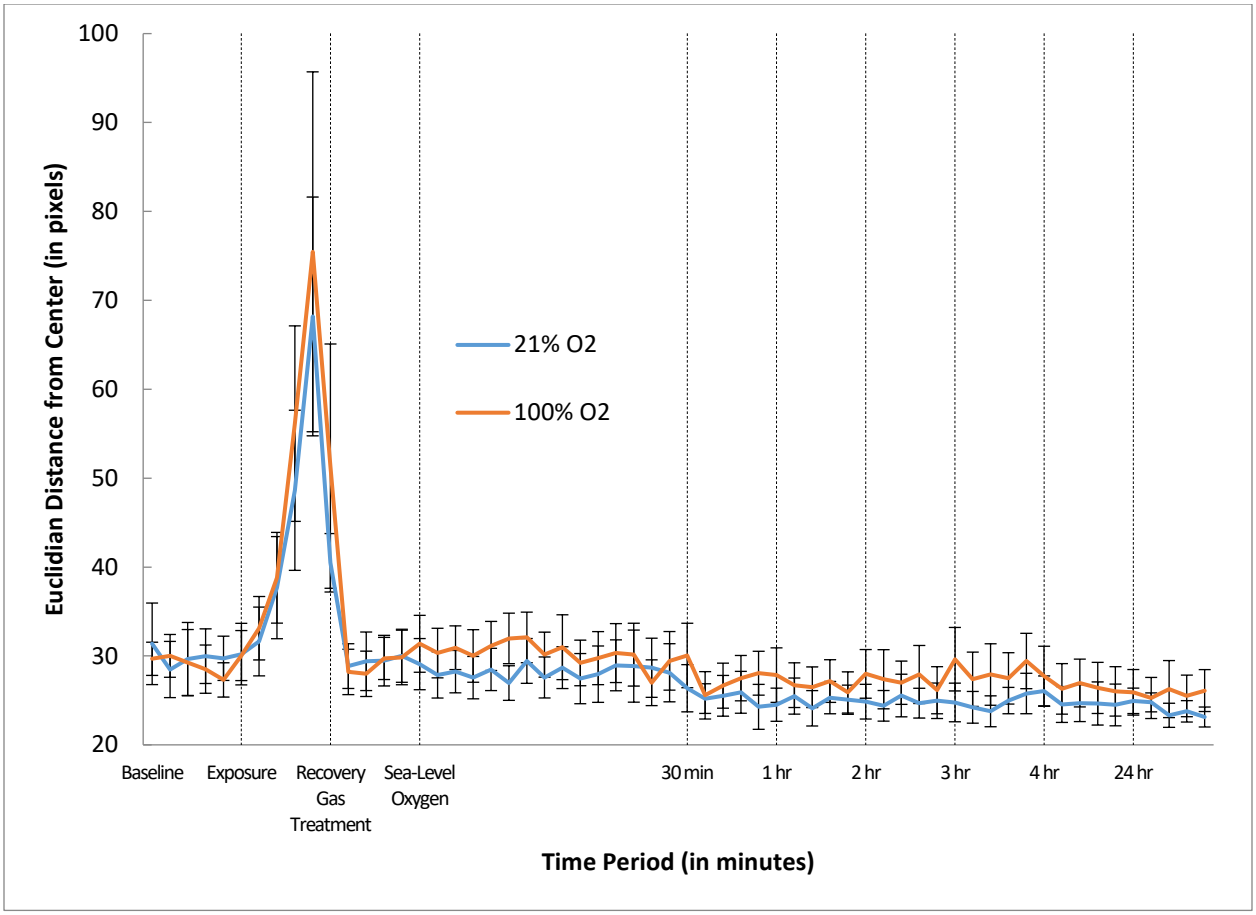

Figure 1. Geometric means of vector errors in the 21% and 100% O_2 recovery treatment groups as a function of time period. Error bars are standard error.

It is evident in the figure that performance in both treatment groups diminished severely during the hypoxic exposure, but returned to baseline levels shortly after the administration of the recovery gas. It is also evident that task efficiency in both groups generally mirrored the other throughout the duration of the investigation. These impressions were confirmed by a 2 (treatments) × 60 (time in minutes) repeated measures ANOVA, which revealed a significant main effect for time, $F(9, 531) = 8.53$, $p < 0.001$. Supplementary *t*-tests examining the values of distance from the target center over time indicated that performance indexed in minutes 8, 9, and 10, the latter half of the hypoxic exposure period, was significantly poorer than that which preceded and was subsequent to the exposure, $p < 0.05$. The main effect for treatment group and the treatment × time interaction were not found to be significant, however, $p > 0.05$.

4.2 Blood O_2 Saturation and NIRS

Blood O_2 saturation levels were examined for differences between groups throughout the task. A paired samples *t*-test confirmed that individuals' O_2 saturations declined to a similar point in both treatment groups (60.15% and 60.09% in the 21% and 100% groups, respectively), which was not found to be significant, $p > 0.05$.

As regional O_2 saturation values indexed by NIRS can vary widely across individuals, rSO_2 values for all subjects were expressed as proportional differences from the sea-level baseline period of time. Mean regional O_2 saturation scores for the 21% and 100% treatment groups are plotted as a function of time in Figure 2.

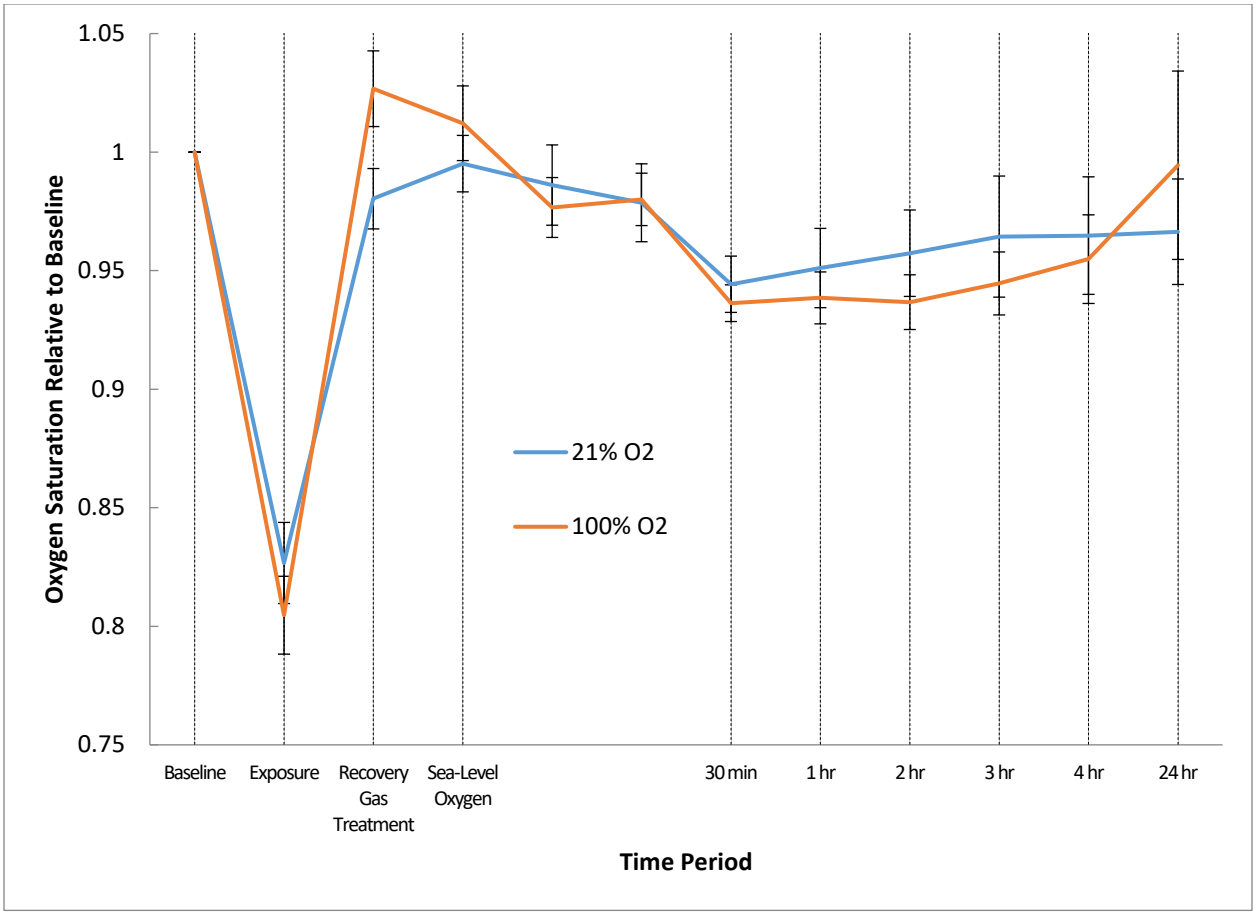

Figure 2. Cerebral O_2 saturation scores in the 21% and 100% recovery treatment conditions as a function of time period. Error bars are standard errors.

A 2 (treatment) × 12 (time) repeated measures ANOVA revealed a significant main effect for time, $F(11, 99) = 15.22$, $p < 0.001$. Post hoc *t*-tests with an alpha level of 0.05 indicated a significant temporal decline in cerebral O_2 saturation during the exposure period, but a subsequent recovery to baseline levels immediately following the administration of the recovery gas, regardless of treatment concentration. However, this recovery was impermanent in that O_2 saturation levels began to decline shortly after the treatment gas administration, fell below baseline levels when indexed during the 30-minute post-exposure assessment, and remained significantly depressed until the fourth hour of examination. The main effect for treatment group and the treatment × time interaction were not found to be significant, $p > 0.05$.

5.0 DISCUSSION

Hypoxia remains a major threat to aviators in modern tactical air platforms and has thus far been implicated in four Class A mishaps and hundreds of hazard reports since 2001. To this point, an emphasis has been placed on the investigation of the consequences of hypoxia with regard to physiology and subsequent cognitive task performance. However, little research has been conducted on the time period following a hypoxic exposure and the time course to recovery until recently. Studies by Phillips and his colleagues have shown that contrary to conventional thought, the negative effects of hypoxia on cerebral O_2 saturation and task performance persist beyond return to sea-level O_2 concentrations [15-17]. Accordingly, the goal of the present study was to examine both a sea-level O_2 concentration and a 100% O_2 concentration (as would be supplied by in-flight emergency systems) while documenting performance throughout the exposure and ensuing recovery period.

In terms of performance efficiency, the overall levels of vector error among subjects in this study were not significantly different before, during, or after the low O_2 exposure, regardless of treatment group. This result was inconsistent with expectation, as it was anticipated that performance in the 100% O_2 concentration treatment group would return to baseline levels significantly more quickly than that measured in the sea-level concentration treatment group. A possible explanation could involve the hemodynamics within the brain following a hypoxic event. Functions that underlie the performance of such a task are supported by the motor and premotor areas of the brain [19-21], and therefore would be among the first to be oxygenated upon the cessation of a hypoxic event, and could conceivably recover at a similar rate regardless of inspired O_2 concentration in a normobaric environment. Along these lines, an analogous explanation could be used when compared to the results indicating a delay in performance recovery found in previous studies. Phillips and his associates employed reaction time tests to gauge performance during their investigations, which have shown activation in a number of brain areas during functional magnetic resonance imaging studies [22]. Consequently, this could potentially necessitate a longer amount of time to adequately oxygenate all involved areas to support pre-exposure performance levels. Alternatively, it is possible that those systems involved with the execution of action while engaged in a reaction time task may simply be more susceptible to the effects that hypoxia has on general perception, thereby negatively influencing the speed at which subjects can respond.

Analysis of the NIRS data appeared to be generally consistent with that reported by Phillips et al. [15,16], pointing toward a recovery of O_2 to near baseline levels when recovering on a normoxic gas mixture, although never completely achieving a value comparable to that recorded during the baseline period. Conversely, recovery on a hyperoxic gas mixture resulted in rSO_2 values above baseline levels for the duration of their administration. Shortly after the hyperoxic gas was replaced by a sea-level supply, however, O_2 saturation declined within the measured region to the point of being significantly less than pre-exposure levels, persisting until measurements were taken 4 hours after the initial exposure. Although performance documented during the affected time periods did not appear to be concomitantly depressed, the area from which readings were taken, the right frontal lobe, may be more involved in the performance of a discrete-response reaction time task than the continuous-response tracking task currently employed. As a result, fluctuations in O_2 saturation found in this area would potentially have little bearing on a task of this type.

The results described above raise the issue of task-characteristic determinants of hypoxia with regard to cognitive performance. The absence of any performance decrements associated with the recovery periods of the current investigation, while unexpected, is noteworthy, as O_2 saturation values mirrored those found in previous examinations. Whatever the reason for this discrepancy, it is plausible to assert that disparate cognitive processes have differing recovery profiles from hypoxia and also react independently to varying concentrations of recovery gas. Thus, rather than viewing the present results as contraindicative of those prior outcomes, they can be interpreted as providing a more complete picture of the hypoxia recovery profile.

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LIST OF ABBREVIATIONS AND ACRONYMS

ANOVA	analysis of variance
NIRS	near-infrared spectroscopy
O_2	oxygen
ROBD	reduced oxygen breathing device
rSO_2	regional cerebral oxygen saturation